

## **ABSTRACT**

Methods of and devices directed to generating a target ligand are disclosed herein. The methods can include, for example, providing a set of models, wherein each model comprises three-dimensional structural information for a ligand or a ligand:macromolecule complex, wherein each ligand comprises a plurality of atoms and a plurality of bonds, and wherein each model is related to the other models of the set by a homologous structural feature; mapping spatial relationships between the models such that the models are superimposed with respect to the homologous structural feature; identifying one or more pairs of matching bonds between ligands of the set, wherein the matching bonds comprise a bond of a first ligand (B1) and a bond of a second ligand (B2) that are superimposed such that (i) an atom at each end of the bond (B1) is within 1.8 angstrom of an atom at each end of the bond (B2), (ii) the bond (B1) and the corresponding bond (B2) are of the same bond order, and (iii) the bond (B1) and the corresponding bond (B2) are related by an angle of 30° or less; selecting a plurality of subsets of atoms and/or bonds from each ligand; wherein each subset comprises a bond and/or, an atom connected to a matching bond; generating and displaying output ligands, each output ligand comprising atoms and/or bonds of a first subset and atoms and/or bonds of a second subset, wherein the first subset and the second subset comprise atoms and/or bonds derived from opposite ends of the a matching bond.